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Larson & Anderson, LLC
P.O. BOX 4928
DILLON, CO 80435

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WESSENDORF, TERESA D	
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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte JEAN GARIEPY and MARK ROBERT BRAY

Appeal 2009-001960[1]
Application 09/601,644
Technology Center 1600

Decided: August 5, 2009

Before FRANCISCO C. PRATS, MELANIE L. MCCOLLUM, and JEFFREY N. FREDMAN, *Administrative Patent Judges*.

PRATS, *Administrative Patent Judge*.

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[1] University Health network and Molecular Templates Inc. are the real parties in interest (App. Br. 1).

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 involving claims to a method for making a cytotoxic mutant protein or pool of proteins. The Examiner has rejected the claims as failing to meet the written description and enablement requirements. We have jurisdiction under 35 U.S.C. § 6(b).

We reverse.

STATEMENT OF THE CASE

Claims 1-7, 9-16, 18, 20, 27-29, 32, 33, 37-41, and 43 stand rejected and are on appeal (App. Br. 2). Claim 1 is representative of the appealed subject matter and read as follows:

> 1. A method for making a cytotoxic mutant protein or pool of proteins from a cytotoxic wild type protein, said mutant protein or pool of proteins having receptor-binding specificity for a receptor that is different from the receptor to which the wild type protein has receptor binding specificity, comprising:
> (A) selecting a heteromeric protein toxin having a toxic domain or subunit and a binding domain or subunit, wherein the heteromeric protein toxin is a ribosome inactivating protein;
> (B) incorporating mutations into DNA encoding the binding domain or subunit of the heteromeric protein toxin to produce a plurality of variant forms of the heteromeric protein toxin;
> (C) generating a library of microorganism clones producing variant forms of the heteromeric protein toxin;
> (D) screening the variant forms of the heteromeric protein toxin of said library against a population of screening cells by (i) isolating clones or pools of clones producing said variant forms of the heteromeric protein toxin, (ii) treating preparations of said population of screening cells with variant forms of the heteromeric protein toxin produced by the isolated clones or pools of clones, (iii) observing the treated preparations of said population of screening cells for toxicity, and (iv) selecting based on the observation of toxicity a cytotoxic mutant protein or pool of cytotoxic mutant proteins that inhibits or kills said population of screening cells to a greater extent than the wild-

type cytotoxic protein, whereby said selected mutant protein or pool of proteins has the different receptor binding specificity that is reflected by the observation of toxicity, wherein the screening cells are insensitive to the selected cytotoxic heteromeric protein toxin at a concentration used in the screening; and
(E) making additional copies of the selected cytotoxic mutant protein or pool of proteins.

The Examiner cites the following documents as evidence of unpatentability:

Smith	US 6,833,131 B1	Dec. 21, 2004
Sheppard	US 2002/0161203 A1	Oct. 31, 2002
D'Andrea	US 2003/0188326 A1	Oct. 2, 2003

M.R. Hartley et al., *Cytotoxic ribosome-inactivating lectins from plants*, 1701 BIOCHIMICA ET BIOPHYSICA ACTA 1-14 (2004).

Lynne M. Roberts et al., *Ribosome-Inactivating Proteins: Entry into Mammalian Cells and Intracellular Routing*, 4 MINI REVIEWS IN MEDICINAL CHEMISTRY 505-512 (2004).

Maria Giulia Battelli, *Cytotoxicity and Toxicity to Animals and Humans of Ribosome- Inactivating Proteins*, 4 MINI REVIEWS IN MEDICINAL CHEMISTRY 513-521 (2004).

Yasufumi Kaneda, *Gene Therapy: A Battle Against Biological Barriers*, 1 CURRENT MOLECULAR MEDICINE 493-499 (2001).

Examination Guidelines on Written Description (uspto.gov/web/menu/written.pdf).

The following rejections are before us for review:

Claims 1-7, 9-16, 18, 20, 27-29, 32, 33, 37-41 and 43 stand rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement (Ans. 3-14).

Claims 1-7, 9-16, 18, 20, 27-29, 32, 33, 37-41 and 43 stand rejected under 35 U.S.C. § 112, first paragraph, "because the specification, while being enabling for methods of for making a cytotoxic mutant protein or pool of Shiga toxin or Shiga-like toxin proteins, does not reasonably provide enablement for making mutants for any heteromeric ribosome inactivating protein with a different receptor binding specificity" (Ans. 14).

WRITTEN DESCRIPTION

ISSUE

The Examiner finds that the genus of cytotoxic proteins recited in the claims is "broad and includes species named in the specification and claimed, such as Shiga toxin, Shiga-like toxins, ricin, abrin, gelonin, crotin, pokeweed antiviral protein, saporin, momordin, modeccin, sarcin, diphtheria toxin and Psudomonas [sic] aeruginosa exotonin A, as well as other species not described, such as snake, lizard, spider and insect venoms" (Ans. 4 (citing Smith and Sheppard)). In contrast, the Examiner finds, the Specification "provides specific embodiments, working or otherwise, only for Shiga-toxin and Shiga-like toxins" (*id.*).

The Examiner further finds that, in using screening cells insensitive to the Shiga and Shiga-like toxins, Appellants' Example 4 used a specific cell line, CAMA-I, because it lacked the CD77 receptor for those toxins (*id.*). In contrast, the Examiner argues, the Specification "does not disclose cell lines that similarly lack the receptors for the other heteromeric protein toxins that constitute the genus" of toxin-insensitive cells recited in claim 1 (*id.*).

Based on these findings, the Examiner contends that the Specification "does not provide a representative number of species to show possession over the entire genus claimed" (*id.* at 5).

The Examiner notes that "the examined claims do not require that the screening cell line lack the receptor recognized by the wild-type toxin" (*id.*). The Examiner further notes that, even with respect to the exemplified Shiga toxin, the Specification does not identify the receptor that the toxin bound, and therefore, "the practitioner would not be reasonably apprised the Appellant[s were] in possession of the claimed invention, in regard to the particular species of Shiga toxin or Shiga-like toxin" (*id.* at 5-6).

Appellants contend that the claims require the use of ribosome inactivating proteins, or RIP proteins, which "represent a class of known and characterized proteins," as evidenced by publications submitted with the Appeal Brief (App. Br. 5, 19 (Evidence Appendix)). Moreover, Appellants argue, the "invention here is a method, not the proteins per se" (*id.*). Thus, the claimed invention takes advantage of the binding properties of RIPs "to provide a method for making proteins that bind to different receptors, but this use requires no knowledge of the starting sequence" of the proteins (*id.*).

With respect to obtaining cell lines useful in the screening process, Appellants urge that "[t]hese cells already exist. All that is required is pairing a cell of interest with an appropriate RIP that does not bind to the surface of that cell as reflected by insensitivity to the toxin" (*id.* at 6). Thus, Appellants urge, [i]n the unlikely event that some cell should possess every surface marker to which an RIP binds, then use of that cell would not fall within the scope of the claims since these cells could not be 'insensitive to

the selected cytotoxic heteromeric protein toxin at a concentration used in the screening' as required in the claims" (*id.* at 6-7).

In view of the positions advanced by Appellants and the Examiner, the issue with respect to this rejection is whether the Examiner erred in finding that claims involving screening methods, which test the toxicity of mutated forms of the known class of RIP proteins against cells lacking sensitivity to the proteins' wild-type forms, lack descriptive support because the examples in the Specification are limited to testing the toxicity of mutated forms of Shiga toxin, and because the Specification describes only a single cell line lacking sensitivity to the wild-type form of the Shiga toxin.

FINDINGS OF FACT ("FF")

1. Claim 1 recites a method for making a cytotoxic mutant protein, or pool of proteins, from a cytotoxic wild type protein. The mutant proteins must have binding specificity for a receptor that is different from the receptor to which the wild-type protein specifically binds.

2. Claim 1 includes the steps of:

(A) selecting a heteromeric ribosome inactivating protein toxin that has a toxic domain/subunit and a binding domain/subunit;

(B) incorporating mutations into the DNA encoding the binding domain/subunit of the toxin to produce a plurality of variant forms of the toxin;

(C) generating a library of microorganism clones that produce the variant forms of the toxin;

(D) screening the variant forms of the toxin from the library against a population of screening cells to determine which of the mutated toxins is toxic to the cells; and

(E) making additional copies of the cytotoxic mutant protein or pool of proteins obtained in step (D).

3. Claim 1 requires the screening process of step (D) to be performed by:

(i) isolating the clones or pools of clones that produce the variant forms of the toxin,

(ii) treating preparations of the screening cells with variant forms of the heteromeric protein toxin produced by clones,

(iii) observing the treated preparations of the screening cell population for toxicity, and

(iv) selecting, based on the observation of toxicity, a cytotoxic mutant protein or pool of cytotoxic mutant proteins that inhibits or kills the population of screening cells to a greater extent than the wild-type cytotoxic protein.

4. Claim 1 also requires the screening cells to be insensitive to the wild-type form of the selected toxin at a toxin concentration used in the screening.

5. The Specification discloses that the method recited in claim 1 allows a practitioner to "screen[] combinatorial protein libraries of the toxin's template to find mutant toxins that kill specific cells or cell types" (Spec. 2).

6. Claim 1 limits the screening process to one that evaluates mutant heteromeric ribosome inactivating proteins.

7. The Specification discloses that the family of heteromeric plant and bacterial toxins "includes examples such as Shiga and Shiga-like toxins, the

E. coli heat-labile enterotoxins, cholera toxin, diphtheria toxin, pertussis toxin, *Pseudomonas aeruginosa* exotoxin A as well as plant toxins such as ricin and abrin" (Spec. 6 (citations omitted)).

8. According to the Specification, "[b]ased on their ability to block protein synthesis, proteins such as Shiga and Shiga-like toxins as well as ricin, abrin, gelonin, crotin, pokeweed antiviral protein, saporin, momordin, modeccin, sarcin, diphtheria toxin and exotoxin A have been referred to as ribosome-inactivating proteins (RIP) (*id.*).

9. Appellants cite a number of publications to support the assertion that RIPs are a class of known and characterized proteins (App. Br. 19 *et seq.* (Evidence Appendix)).

10. While the Examiner cites Smith and Sheppard as evidence that the claims encompass a number of toxins not mentioned in the Specification (Ans. 4), the Examiner does not dispute the fact that RIPs are a class of known and characterized proteins.

11. Claim 1 does not limit the screening cells to any particular cell type or cell line.

12. The Specification states that "[t]he target cell may be a tumour cell, for example, a breast cancer cell" (Spec. 3).

13. The Specification discloses examples in which Shiga toxin mutants are tested against two breast cancer cell lines, SK-BR-3 and CAMA-I (*id.* at 17-23). Of the two cell lines, only the CAMA-I line meets the requirement in claim 1, that the screening cells be insensitive to the wild-type toxin, in this case Shiga toxin (*id.* at 22). Three Shiga toxin mutants were shown to have greater cytotoxicity to CAMA-I than wild-type Shiga toxin (*id.*; *see also* Figure 6).

14. The Specification does not provide working examples in which any other RIPs are tested against any other cell lines.

15. The Examiner cites Roberts as evidence that the RIP ricin can bind to a number of different cell surface glycoproteins, and that therefore "[t]he practitioner would not envision that the Appellant had process [sic, possession] of mutant proteins that have different receptor specificity" (Ans. 8).

16. The Examiner cites Battelli as evidence that the interaction between cells and RIPs was more complicated than could be predicted based on structure, and that, accordingly, "it is clear that the genus of RIPs is heterogeneous, unpredictable, and complicated in the mechanism of action. Therefore, one of skill in the art would not envision that the Appellant had possession of the invention as now claimed" (Ans. 9).

17. Apparently noting that certain claims encompassed using the claimed screening method to prepare gene therapy vectors, the Examiner cites Kaneda as evidence that gene therapy is not without its problems, and "that various gene delivery systems, including adenovirus systems, have well known limitations that have prevented safe and successful methods of gene therapy" (*id.* at 10). Kaneda also discloses, however, that gene therapy has proven successful in certain circumstances (Kaneda 493).

18. The Examiner cites D'Andrea as evidence that a skilled artisan "would appreciate that insensitivity to a toxin might result from a variety of reasons, such as amplification of the gene of a target protein or an enhanced toxin efflux mechanism in the insensitive cell" and that therefore, "[w]ithout recognition of the nature of the receptor to which the mutated protein binds,

one of skill in the art would not be reasonably apprised that the receptor was different, as required by the claims" (Ans. 12).

PRINCIPLES OF LAW

The written description requirement "serves a teaching function, as a quid pro quo in which the public is given meaningful disclosure in exchange for being excluded from practicing the invention for a limited period of time." *Ariad Pharmaceuticals, Inc. v. Eli Lilly and Co.*, 560 F.3d 1366, 1371 (Fed. Cir. 2009) (quoting *Univ. of Rochester v. G.D. Searle & Co.,* 358 F.3d 916, 922 (Fed. Cir. 2004)).

To meet the initial burden of establishing a prima facie case of unpatentability based on a lack of written description, the Examiner must "present[] evidence or reasons why persons skilled in the art would not recognize in the disclosure a description of the invention defined by the claims." *In re Alton*, 76 F.3d 1168, 1175 (Fed. Cir. 1996).

While there is some flexibility in how applicants may comply with the written description requirement, "the patent specification [must] set forth enough detail to allow a person of ordinary skill in the art to understand what is claimed and to recognize that the inventor invented what is claimed." *Rochester*, 358 F.3d at 928.

However:

> A claim will not be invalidated on section 112 grounds simply because the embodiments of the specification do not contain examples explicitly covering the full scope of the claim language. That is because the patent specification is written for a person of skill in the art, and such a person comes to the patent with the knowledge of what has come before. Placed in that context, it is unnecessary to spell out every detail of the

> invention in the specification; only enough must be included to convince a person of skill in the art that the inventor possessed the invention and to enable such a person to make and use the invention without undue experimentation.

Falkner v. Inglis, 448 F.3d 1357, 1366 (Fed. Cir. 2006) (quoting *LizardTech, Inc. v. Earth Resource Mapping, PTY, Inc.*, 424 F.3d 1336, 1345 (Fed.Cir.2005)); *see also Capon v. Eshhar*, 418 F.3d 1349, 1359 (Fed. Cir. 2005) ("It is not necessary that every permutation within a generally operable invention be effective in order for an inventor to obtain a generic claim, provided that the effect is sufficiently demonstrated to characterize a generic invention.").

In addition to relying on the knowledge of a skilled artisan, whether a disclosure provides adequate descriptive support "depends upon the context of the claimed invention." *Ariad*, 560 F.3d at 1372. Thus, for example, in *Ariad* our reviewing court found that claims broadly directed to methods of reducing NF-KB-mediated effects in cells lacked descriptive support where the specification hypothesized that three types of molecules would be able to accomplish the claimed function, but rather than providing actual working examples, simply made "mere mention of a desired outcome." *Id.* at 1375; *see also Rochester,* 358 F.3d at 927-28 (claims reciting use of compound capable of selectively inhibiting prostaglandin H synthase-2 held to lack written description where specification disclosed screening method, but no compounds having the claimed activity).

In contrast, in *Falkner v. Inglis*, the court affirmed this Board's finding that claims to a modified pox virus vaccine had descriptive support, despite the fact that the specification focused on viruses other than pox virus,

provided no examples directed to pox virus, and discussed pox virus only in general terms relating to the inventive disclosure. *See Falkner*, 448 F.3d at 1364-67. Given extrinsic evidence that the critical portions of a pox virus in relation to the disclosure were well known, the court reasoned that the disclosure was sufficient to support the claims. *Id.; see also Capon v. Eshhar*, 418 F.3d at 1354-58 (court vacated Board's finding of lack of descriptive support for claims directed to combinations of known genes where specifications failed to provide explicit sequence disclosures, but where genes' sequences were known in the art); *also Noelle v. Lederman*, 355 F.3d 1343, 1349 (Fed. Cir. 2004) ("[A]s long as an applicant has disclosed a *fully characterized* antigen, either by its structure, formula, chemical name, or physical properties, or by depositing the protein in a public depository, the applicant can then claim an antibody by its binding affinity to that described antigen." (internal quotations omitted)).

Ultimately, therefore, the test for determining whether a specification is sufficient to support a particular claim "is whether the disclosure of the application relied upon 'reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter.'" *Ralston Purina Co. v. Far-Mar-Co, Inc.,* 772 F.2d 1570, 1575 (Fed. Cir. 1985) (quoting *In re Kaslow,* 707 F.2d 1366, 1375 (Fed. Cir. 1983)).

ANALYSIS

We agree with Appellants that the Examiner erred in finding that the claims lack descriptive support. In contrast to claims requiring a specific therapeutic compound unknown in the prior art and undefined in the Specification, the process of claim 1 is a screening method which, by its

nature, seeks to identify such compounds. Moreover, the steps in the process are clearly defined in both the claim and Specification.

Although not recited as the first step, it is evident that to practice the invention one must initially select a cell type or cell line of interest that is amenable to the screening method (*see* FF 2, 3). As noted above, the Specification states that tumor cells, including breast cancer cells, are of particular interest (FF 12). Given the general thrust in the Specification that the method is for identifying chemotherapeutic agents for killing undesirable cells (*see* FF 5), a skilled artisan would thus have reasoned that the process would be useful for screening other known cancer cells or tumor cells. Simply put, if the practitioner seeks to find agents capable of killing lung cancer cells, then the practitioner would use a primary or immortalized lung cancer cell line of interest as the screening cells.

To practice the method recited in claim 1, the practitioner also must determine whether the cells of interest lack sensitivity to the wild-type form of a heteromeric ribosome inactivating protein toxin, or RIP (*see* FF 4). The Examiner takes issue with the fact that the Specification exemplifies only a single cell line that lacks sensitivity to a single RIP (Ans. 4).

However, the record contains significant evidence, and the Examiner does not dispute, that RIPs are a recognized and characterized class of proteins (FF 7-10). Thus, in the instant case, if the practitioner seeks to find agents capable of killing lung cancer cells, then the practitioner screens the cell line of interest against RIPs, an art-recognized class of proteins, to determine if the cell he or she wants to kill is insensitive to any of them. As Appellants point out, if a particular cell line is sensitive to every RIP tested, then that cell line is not amenable to the claimed invention.

In the process of claim 1, once the practitioner obtains an RIP to which the target cells are insensitive, a library of variant forms of that RIP is generated by creating mutations in the receptor binding subunit (FF 2), and the cells are screened to determine which, if any, of the variant forms of the RIP are cytotoxic to the cells of interest (FF 2, 3). The cytotoxic forms of the RIP are then selected and additional copies made (*id.*).

The Examiner urges that, given the complexity and unpredictability in the RIP-receptor binding association, Appellants' Specification fails to demonstrate generic possession of RIP variants that have different receptor specificity than their wild-type counterparts, as required by the claim 1 (*see* FF 15-18). We are not persuaded that the Specification fails to adequately support the claims.

As noted above, claim 1 is directed to a screening process, which is investigatory by nature, and also lacks predictability by its nature. Thus, rather than using solely functional language to generically recite a therapeutic compound whose structure has not been described in the Specification, *see, e.g., Rochester,* 358 F.3d at 927-28, claim 1 recites a specific series of enumerated steps using art-recognized materials to identify proteins having specifically defined properties. The Specification discloses that the screening process in fact identified three mutant proteins having the desired properties (FF 13).

In sum, because the Specification clearly sets out the steps required to practice the method recited in claim 1, and because a skilled artisan would understand what materials would be useful in the process, we reverse the Examiner's rejection of claim 1 as lacking written description.

Claim 18 depends from claim 1, and recites "[a] method for identifying therapeutic proteins having binding specificity for a target cell." Claim 18 requires performing the process of claim 1, and the additional steps of screening the obtained cytotoxic mutant RIPs against the target cells and also against non-target cells and by treating a preparation of target and a preparation of non-target cells with said cytotoxic mutant protein or pool of proteins, and "selecting a therapeutic protein or pool of therapeutic proteins that are effective to inhibit or kill said target cells and that are less effective at inhibiting or killing said non-target cells than at inhibiting or killing said target cells."

Thus, claim 18 adds to claim 1 a step in which the cytotoxic mutant RIP is tested to see if it is cytotoxic to non-target cells. Because the Examiner does not point to, and we do not see, any inadequacy in the Specification's description of the additional steps recited in this embodiment, we also reverse the Examiner's rejection of claim 18 as lacking written description.

Claim 27 depends from claim 1 and recites "[a] method for constructing a diagnostic probe for detecting the presence of a cell surface marker." Claim 27 requires performing the process of claim 1, and then "preparing a diagnostic probe by labeling the selected cytotoxic mutant protein in a manner which maintains the ability of the binding domain or subunit of the selected cytotoxic mutant protein to specifically bind to the cell surface marker."

Thus, claim 27 adds to claim 1 a step in which a detectable label is attached to the cytotoxic mutant RIP. Because the Examiner does not point to, and we do not see, any inadequacy in the Specification's description of

the additional steps recited in this embodiment, we also reverse the Examiner's rejection of claim 27 as lacking written description.

Claim 32 recites "[a] method for making a targeted medicament for delivery to a target cell having a cell surface marker, said targeted medicament comprising a binding portion and a medicament portion."

The Examiner urges that this embodiment encompasses making gene therapy agents, and that gene therapy is unpredictable (Ans. 10). This fact does not persuade us that the Specification's description of this embodiment is inadequate.

The process is accomplished essentially by performing the steps recited in claim 1 to obtain a mutant RIP that binds to the cell surface marker, after which the binding portion of the RIP is sequenced and then combined with the medicament. As discussed above, we do not agree with the Examiner that the screening process recited in claim 1 lacks descriptive support in the Specification. Moreover, because the claim encompasses combining known medicaments with the mutant RIPs obtained by the screening method, we do not agree that a person skilled in the art would fail to recognize that Appellants possessed the claimed synthetic method.

Regarding the issue of preparing gene therapy agents, we note that Kaneda discloses that certain applications of gene therapy have proved successful (FF 17). However, a broad claim does not lack written description merely because it encompasses inoperative embodiments. *Capon*, 418 F.3d at 1359 ("It is not necessary that every permutation within a generally operable invention be effective in order for an inventor to obtain a generic claim, provided that the effect is sufficiently demonstrated to characterize a generic invention.").

Thus, we agree with Appellants that the Examiner has not made a prima facie case of lack of written description with respect to claim 32. We therefore reverse the Examiner's written description rejection of that claim.

Claim 37 recites a method having the same basic screening steps recited in claim 1, except that the method is for obtaining nucleic acids that encode the mutant cytotoxic RIP. Thus, the final step in claim 37 recites making additional copies of the nucleic acids that encode the cytotoxic mutant protein, rather than making copies of the protein. Therefore, for reasons essentially the same as discussed above with respect to claim 1, we agree with Appellants that the Examiner has not made a prima facie case that claim 37 lacks descriptive support in the Specification. Accordingly, we reverse the Examiner's written description rejection of that claim.

In sum, for the reasons discussed above, we reverse the Examiner's rejections of claims 1, 18, 27, 32, and 37, and their dependent claims, as failing to meet the written description requirement of 35 U.S.C. § 112, first paragraph.

ENABLEMENT

ISSUE

Claims 1-7, 9-16, 18, 20, 27-29, 32, 33, 37-41 and 43 stand rejected under 35 U.S.C. § 112, first paragraph, "because the specification, while being enabling for methods of for making a cytotoxic mutant protein or pool of Shiga toxin or Shiga-like toxin proteins, does not reasonably provide enablement for making mutants for any heteromeric ribosome inactivating protein with a different receptor binding specificity" (Ans. 14).

Applying the oft-cited factors from *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988), the Examiner finds that the claims broadly encompass

making mutants of any RIP protein, and that the receptor to which the mutated RIP binds encompasses "virtually any biological molecule" (Ans. 16). Conversely, the Examiner finds that the Specification only exemplifies mutating Shiga toxin, and the examples do not establish that the obtained mutants fail to bind to the Shiga toxin's receptor (*id.*).

The Examiner further finds that "the genus of RIPs is heterogeneous, unpredictable, and complicated in the mechanism of action," as evidenced by Battelli (*id.* at 17). Thus, despite the high skill level of an ordinary artisan, the Examiner concludes that the amount of experimentation required to practice the full scope of the claimed invention would be undue (*id.* at 19).

Appellants contend that the process recited in claim 1 would not require undue experimentation "since claim 1 itself is essentially the instructions for performing the method of the invention" (App. Br. 8).

In view of the positions advanced by Appellants and the Examiner, the issue with respect to this rejection is whether the Examiner erred in concluding that an ordinary artisan viewing Appellants' Specification at the time of filing would have had to experiment unduly to practice the full scope of the claimed subject matter.

PRINCIPLES OF LAW

The Examiner bears the burden of establishing that practicing the full scope of the claimed subject matter would have required undue experimentation. *In re Wright*, 999 F.2d 1557, 1561-62, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993) ("[T]he PTO bears an initial burden of setting forth a reasonable explanation as to why it believes that the scope of protection

provided by that claim is not adequately enabled by the description of the invention provided in the specification of the application.").

> Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. . . . The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed.

In re Wands, 858 F.2d at 736-37 (citations omitted).

Moreover, "[working] examples are not required to satisfy section 112, first paragraph." *In re Strahilevitz*, 668 F.2d 1229, 1232 (CCPA 1982). For example, in *Falkner v. Inglis*, the court affirmed this Board's conclusion that claims to a modified pox virus vaccine were enabled, despite the fact that the specification focused on viruses other than pox virus, provided no examples directed to pox virus, and discussed pox virus only in general terms relating to the inventive disclosure. *Falkner,* 448 F.3d at 1365.

Thus, as noted in *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1334 (Fed. Cir. 2003):

> The enablement requirement is often more indulgent than the written description requirement. The specification need not explicitly teach those in the art to make and use the invention; the requirement is satisfied if, given what they already know, the specification teaches those in the art enough that they can make and use the invention without "undue experimentation."

ANALYSIS

We agree with Appellants that the Examiner did not make a prima facie case that practicing the full scope of the claims would have required

undue experimentation. As discussed above, the claimed processes all include the screening steps recited in claim 1, or a close variation.

We note, because the outcome is neither clear nor assured, that the claimed screening methods include an element of unpredictability by their nature. We also note that a screening method can require significant amounts of experimentation.

However, a method does not lack enablement merely because its practice requires a lot of experimentation. *See Wands*, 858 F.2d at 737 ("The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed .").

In the instant case, as discussed above, the claims are limited to using RIPs, which are a known and recognized class of proteins (FF 8-10). The Specification discloses that the screening cells can be tumor cells, with particular emphasis on breast cancer cells (FF 12). As also discussed above, an ordinary artisan would understand that some testing would be required to determine which, if any, RIPs lack cytotoxicity toward the cell line of interest.

Thus, an ordinary artisan would understand which proteins are to be mutated and tested, and would also understand and be able to determine through simple testing methods which types of tumor cells were amenable to the described screening methods. Given these facts, and the straightforward nature of the screening steps required in the claimed methods, we do not agree with the Examiner that undue experimentation would be required to

practice the full scope of the claims. We therefore also reverse the Examiner's enablement rejection.

SUMMARY

We reverse the Examiner's rejection of claims 1-7, 9-16, 18, 20, 27-29, 32, 33, 37-41, and 43 stand rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement.

We also reverse the Examiner's rejection of claims 1-7, 9-16, 18, 20, 27-29, 32, 33, 37-41, and 43 under 35 U.S.C. § 112, first paragraph, as failing to enable the full scope of the claimed subject matter.

REVERSED

alw

LARSON & ANDERSON, LLC
P.O. BOX 4928
DILLON CO 80435